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ABSTRACT

The degree to which under nourishment exists in a local community such as San Diego, California, and in the U.S. at large, and whether it is severe enough to interfere with brain development is the focus of this report. After establishing criteria for nutrition intake that would represent unambiguous jeopardy to brain development, these criteria are applied to the two best available sources of nutritional and developmental evidence based on large and presumably representative populations in the U.S. Results indicate that, as of 1970, more than two million pregnant women, infants, and children under four years of age are under nourished to such a severe degree that the brain development of the unborn and young child is in jeopardy. Evidence is also found that indicates that nutritional intake, blood and urinary bio-chemistry, and anthropometric measures are deficient but tend to be ameliorated as family incomes rise. The presumptive outcome of such severe under nutrition may be the introduction into the U.S. school systems and ultimately into adult society between one-third and one-half million youngsters annually who may be lastingly or permanently handicapped in relation to functions that depend upon brain structure and organization. The criteria used for predicting jeopardy to brain development deliberately selected to be conservative should be reconsidered. (Author/AM)

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# PROBABILITIES OF UNDERDEVELOPMENT OF THE HUMAN BRAIN AS A CONSEQUENCE OF UNDERNUTRITION IN THE UNITED STATES

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This paper, for reasons that will become evident from its contents, is dedicated to the American ideals for sharing abundance that are celebrated on the traditional holiday of THANKSGIVING.

This investigation into the relations between nutrition intake and brain development was undertaken in the Institute for Information Systems and the Department of Neurosciences at the University of California at San Diego, as a result of student initiative. It received strong collaborative support from the Department of Nutritional Sciences, of the University of California at Berkeley. Co-authors of this report are: John S. MacGregor and Gary J. Fisher, graduate students, Doris H. Calloway, Professor of Nutrition, UCB, and A. Baird Hastings, Research Associate, UCSD.

Our point of departure was the evidence from animal and human studies that undernutrition may be a significant source of underdevelopment of the brain. Our students wanted to know whether there might be undernourishment in our local community, San Diego, and in the United States, to a degree that would be severe enough to interfere with brain development.

Their first question was: What degree of undernourishment would almost certainly lead to underdevelopment of the human brain? We did not seek to learn what would be the threshold of undernutrition effects: that would be much too difficult. We wanted to develop criteria for nutrition intake that would represent unambiguous jeopardy to brain development.

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An answer was not available in the literature. We therefore asked Dr. Calloway, who has served several years on the Food and Nutrition Board of the National Academy of Sciences-National Research Council, and on the World Health Organization and Food and Agriculture committees internationally, how to proceed. The literature suggested that brain development is somewhat protected compared with other tissues. That is, on a gram-per-gram basis, the nervous system may not lose quite as much weight as say, muscle, liver, or bone. But the difference in percentage loss is not very great. It is highly likely that a loss, in mass, of brain tissue could be more devastating than a similar gram-per-gram loss from other tissues. This is because the brain is made up of cells whose functions are interdependent, not additive but multiplicative, in some very complicated way. For example, if red blood cells were diminished by 20%, you would know that the oxygen carrying capacity of the blood had been reduced by 20%. If the brain were diminished by a similar percentage, that loss might be far more deleterious.

Dr. Calloway suggested that we consider, conservatively, that loss of brain tissue ran pari passu with losses from other tissues, as a consequence of undernutrition. She suggested that we use some fraction or percentage of Recommended Daily Allowances (RDA) so that our criteria could then be applied to any individual, by age, sex, size and occupation. She recommended that we select 70% of energy RDA as one criterion. That percentage represents two standard deviations (s.d.) below the average daily energy requirement. This would mean that only 2.5% of any normal, adequately nourished, healthy population could be expected to be able to maintain normal body weight and to maintain growth on a continuing nutritional intake at that level.

In the U.S., the RDA for energy is established by the Food and Nutrition Board of the NAS-NRC to be equal to the average daily energy requirement. The reason for this conservatism is that, in the U.S. at least, there is a conspicuous health hazard from overeating. Therefore, 70% of RDA is 2 s.d. below average daily energy requirements.

For protein, Dr. Calloway suggested that we set our criteria at 40% of protein RDA. This would be 4 s.d. below the RDA for protein

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as established by the Food and Nutrition Board. The Board has proposed that the protein intake be recommended at 2 s.d. above average daily requirements. Perhaps the two most important reasons for this are that protein containing foods are relatively more expensive, hence there is some natural resistance to their purchase; and, more importantly, that the hypothalamic and other meahanisms relating to food appetites are not effectively responsive to the needs for protein. Four s.d. below RDA for protein, therefore, is exactly equal to the criteria set for energy intake, namely, 2 s.d. below average daily requirement.

* * *

We applied these nutrition intake criteria to the two best available sources of nutritional and developmental evidence based on large and presumably representative populations in the U.S. These were the Ten State Nutrition Survey (TSNS), conducted by the Health Services and Mental Health Administration of the Center for Disease Control, Department of Health, Education and Welfare, and A Study of Nutritional Status of Preschool Children in the United States (PNS), carried out collaboratively by Ohio State University and the University of Georgia. These two surveys were designed and conducted independently during the period 1968-1970. We were privileged to have access to the statistical working tapes from both surveys. We applied the brain jeopardy criteria to the nutritional, medical, biochemical, anthropometric and socioeconomic data contained in the tapes from the two surveys. Our analyses relating to brain development indicate that the two surveys strongly corroborate each other in respect to this problem.

At 2 s.d. below average daily requirements, for energy and/or for protein, only 2.5% of any normal, adequately nourished, healthy population would be able to sustain normal body weight and growth. In 97.5% of such a population, we could expect abnormal weight loss or stunting of growth.

[Slide 1]

When these criteria were applied to the two surveys, it was found that nearly 60% of all pregnant women living below the Federally defined poverty level of income were in jeopardy, as of 1970,

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and that the 95% confidence range lay between 51% and 67%. This means that between half and two-thirds of all pregnant women living in poverty would be expected to be in jeopardy for brain development in their unborn child. The impact would be greatest during the third trimester of pregnancy and that period would be affected by previous undernutrition. The placenta could also be underdeveloped and thus risk greater interference with growth and development.

At 1-2 times the poverty income level, and at 2-3X that level of income, there were still about 45% of pregnant women in jeopardy (47% and 44% respectively).

When these percentages are applied to income data in the 1970 U.S. Census, we find that nearly a quarter of a million pregnant women living in poverty (240,000+) and approximately a third of a million of those living at 1-2X poverty (360,000+) and at 2-3X poverty (340,000+) were ingesting less than the brain jeopardy criterion for energy intake. The overall total of women in jeopardy within these three low income levels was greater than 900,000 (945,000+).

Examining this table further, we find that 43% of pregnant women below poverty were ingesting below another s.d. removed from average daily requirement for energy. Twenty-five percent of pregnant women living in poverty were ingesting less than four s.d. below average daily requirements. Forty-six percent, nearly half of all pregnant women living in poverty, were ingesting less than 70% of RDA for both energy and protein. Fourteen percent were ingesting less than 40% of their RDA for protein, that is, below jeopardy criterion for protein as well as energy. At some low level of intake, protein cannot be utilized as protein, but must be burned for its energy contribution.

[Slide 2]

Using part of this same table, now projected in graphic form, we found that infants and children were considerably better off than the pregnant women; yet they still showed 18-24% of their populations below jeopardy criterion for energy within the poverty population and something like half of those percentages among groups living

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near but above the poverty level of income. Following the percentages presented and applying them against the 1970 U.S. Census data, we found more than 1 million infants and children (1.18 million) below age four (TSNS) and more than 1 million children aged 1-4 years (no infants counted; 1.01 million, PNS).

By these criteria, the total number of pregnant women, infants and young children living below poverty and near poverty levels of income who are in jeopardy for brain development exceeds two million individuals (2.1 million projected on the basis of TSNS alone, and 2.3 million when the evidence from both surveys is consolidated).

The students then asked, given low nutrition intake amongst pregnant women in low income groups, what is the incidence of low birth weight?

[Slide 3]

Among families living below the poverty level of income (PNS) more than 17% of the newborn are below the third percentile for birth-weight, 14% in excess of expectation at the low birthweight end of the scale. Among children born of families living at 1-2X poverty, there are nearly 11% in excess of expectation at the 3rd percentile. Among children born in families living between 2-3X poverty, there is an incidence of 8% in excess of expectation at the 3rd percentile. In children living near but above the 3X poverty level of income, there is a 6% occurrence of birth weights below the 3rd percentile, double the expectancy. The total number of low birth weight newborn in the U.S. in 1970, as a presumed consequence of undernutrition, as estimated from the PNS, was more than 380,000. It is, moreover, appropriate to recall that low birthweight is associated with some 90% of infant mortality.

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A further evidence of severe, chronic undernutrition affecting pregnant women and infants and children (TSNS), and young children (PNS), is illustrated by the results of biochemical tests applied to blood and urinary constituents. Hemoglobins were low, meaning below 10.5 gm% in 15% of pregnant women reported as ingesting below brain

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jeopardy criteria, and 21% were low among TSNS infants and children, with 8% deficient, meaning below 9 gm% hemoglobin, and 9% low among PNS children 1-4 years of age, and 3% deficient. The hematocrits were slightly less affected. Transferrin saturation was deficient in 19% of pregnant women ingesting below brain jeopardy criteria. Deficient transferrin saturation means below 15% saturation. There was a 53% deficiency in PNS children.

Nearly three-quarters of pregnant women ingesting below the brain jeopardy energy criterion showed low serum albumin (below 4 gm% in the first trimester, or below 3.5 gm% in the second and third trimesters, and one-quarter of them were deficient, that is, below 3 gm%. Red cell folacin was low, that is below 160 ngm/ml in 16% of this population of women, with 12% deficient, that is, below 140 ngm/ml. Seventeen percent of the TSNS infants and children were deficient. Viatmin A and urinary riboflavin were also low and deficient in a conspicuous percentage of these populations. Note that the criteria for low and deficient for all of these blood and urinary constituents are clearly conservative, so the homeostatic mechanisms for their regulation have already been overwhelmed.

We must acknowledge, therefore, that among people ingesting less than the energy criterion relating to brain development, there is a notable depletion of biochemical constituents relating to nutrition and metabolism.

* * *

We have found thus far that a large number of pregnant women, infants and children are eating less than we think they should to have a brain product that lives up to their genetic potential. We have found also that this same population shows a conspicuous degree of biochemical deficit due to insufficient nutritional intake, an independent measure of deprivation. The products of gestation in this population includes an exceptionally high incidence of small birthweight children. Each of these three factors appears to become more normal with each increase in levels of income.

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Now we shall examine evidence relating to anthropometry among infants and children as measured in these two comprehensive nutritional surveys. Are the apparently undernourished infants and children subnormal in their growth achievements?

To begin with, it is obvious that measures of weight, height, and head circumference are again independent measures. As you might predict from the tendency to low birthweights, the infants and children in these surveys show a large percentage of physical stunting.

[Slide 5]

Among infants and children living in poverty, more than 1300 in the TSNS (1382), there were 10.6% below the 3rd percentile for weight, 23.3% below the 10th percentile, 41.4% below the 25th percentile, etc. For height, there were 15.8% below the 3rd percentile, 29.2% below the 10th percentile, 45.9% below the 25th percentile, etc. The gravest deficits, however, relate to measurements of head circumference. There were 17.3% below the 3rd percentile, 33.7% below the 10th percentile, 51.6% below the 25th percentile. Altogether, the profile of head circumferences among infants and children living below the poverty level of income, regardless of testimony relating to nutritional intake, was found to be so low in comparison with healthy, well-nourished standard populations, that the chance of this group being a normal population is less than one in one million!

Examination of the categories of infants and children (TSNS) living between 1-2X poverty and between 2-3X poverty shows that as income rises, stunting decreases. The shift from one to the next level of income indicates 14.3%, 7.8%, and 3.7% in excess of the 3rd percentile -- a decrease in rate of presumably stunted brain development to one-half and one-third, with the succession of two steps of improvement in family income.

We have calculated the significances among these TSNS anthropometric comparisons as seen in the following statistics:

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The probability of

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The probability of infants and children from the TSNS representing a normal population for weight and for height is less than .005. As noted above, the chances of this group fitting the standard population for head circumference is .000001! At each of the higher income levels, these distinctions diminish, but they are still extraordinary as regards head circumference. For example, at 1-2X poverty, the head circumferences have a p value of less than .0004. Note that the below poverty level income group is statistically significantly distinguished from teh 1-2X poverty and 2-3X poverty group, but the distinctions between these latter two groups show only a stunting in height among the relatively impoverished, $p < .002$.

[Slide 7]

The table shows comparable data from the PNS for children 1-4 years of age. They also are stunted in all three anthropometric parameters. The percentages closely corroborate those from the TSNS. [Slide 8] The higher income levels show a trend toward normalcy in all anthropometric measures, although the differences between income groups is less marked. The head circumferences of children 1-4 years of age, that is not counting infants, living below the poverty level have a probability of matching the standard population of less than three in a million! The head circumference data, relating solely to the excesses beyond expectations at the 3rd percentile, are presented graphically in the next slide.

* * * * * * *

We have established what we consider to be conservative criteria relating brain growth and development to nutritional intake, and have supplied these criteria to two independent, national nutrition surveys. We have found that, as of 1970, a large number of

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pregnant women (nearly 60% of those living below the poverty income level) were in jeopardy for development of the brain in their unborn children.

Although infants and children are somewhat better nourished than the pregnant women, they display, along with the women, biochemical evidence of chronic, severe undernutrition. Moreover, they are stunted in height, weight and especially in head circumference. For these groups in apparent jeopardy, the incidences of deficiencies in nutrition intake, blood and urinary biochemistry, low birthweight, bodily stunting, and underdevelopment of head size, for stepwise rises in family income show stepwise normalization of measures, from poverty levels of income to above three times the poverty income level.

* * *

The following comments may be appropriate:

A. It is likely, on the basis of extensive studies of normal, well-nourished, healthy populations in the U.S. that head size does not show any statistically significant correlation with intelligence and achievement. However, the available evidence on chronically, seriously undernourished populations suggests that both the unborn and the young child are stunted, that they do not live up to their genetic potential for brain development, and that they are less intelligent on the average. The probability exists that small head size induced by any of a variety of non-genetic factors, of which undernutrition is one, is likely to be accompanied by reduction in intelligence. This probability needs to be examined in a relatively homogeneous population over a long enough time to answer the question definitively. To accomplish this, no food or nutritional supplementation need be withheld. Whenever a nutritional or feeding program may be introduced into a population in jeopardy, some of the children will be at vulnerable stages of brain development, <u>in utero</u>, in i..ancy and young childhood, and other children will have passed part or all the period in which nutritional rehabilitation might be

effective. These children can be studied as reasonable "controls" by being given similar nutritional supplementation and treatment. Some individuals may be found to be relati ely well matched among children in the same neighborhoods and eve n in the same famiies. Yet, until now, the question must be held open, whether undernutrition that leads to underdevelopment of the human brain also leads to underachievement in life. This is an all important, ultimate, and as yet unsatisfactorily answered question. With this question still unanswered, one might suppose that it is a matter of indi ference wehther the brain grows to its full genetic potential o not. But this assumption has not attracted anyone with whom we have discussed this subject.

B. Undernutrition affecting brain development is accompanied by many other depressing and interfering environmental factors from which it is extremely difficult, if not impossible, to isolate particular factors that may be instrumental in affecting brain growth, and especially difficult to isolate those that may be inhibiting the flowering of intelligence. But it can be said, without peradventure of doubt, that nutritional factors may be among the simplest and most readily adjusted of all environmental factors that could be corrected in respect to the lives of these individuals. Remedy is feasible in the form of nutritional supplementation, variable according to taste and requirements, but offering, as if by prescription, a high vitamin, high calorie, high protein canned mixture.

Dr. Paulus Zee, at the St. Jude Hospital in Memphis, Tennessee, has done exactly this, with a population of undernourished pregnant women, infants and children. With regard to head circumferences, his infants and children were statistically like the groups represented in the TSNS and PNS. For example, Dr. Zee reported identical percentages in excess of the 3rd percentile. In Dr. Zee's experience, such supplementation, given during the first year of life, leads in many children to a growth spurt of the brain and skull. The skull sutures may even open up again to accommodate the rapid

brain growth. Such children escape from their percentile cohorts in growth progression, join higher percentile groups and continue their development with a larger brain than would have been expected without such nutritional intervention. Of course, the best results have been found by Dr. Zee by giving the nutrition supplementation to the pregnant women. This results in a reduction in the excess of low birthweight children and reduced stunting in the children, including normalization of their head circumferences. The brain growth spurt encountered by Dr. Zee is prima facie evidence that the brain was not able, under conditions of undernutrition, to live up to its genetic potential.

C. It has been asserted that one of the accompaniments of low income status, low achievement and low intelligence affecting such a population may arise from inadequate genetic material. We have no direct evidence relating to this point, but we do have cogent indirect evidence suggesting that whatever may be the extent and degree of the postulated genetic differences between the populations under consideration and standard populations, the genetic differences do not appear compelling in explanation of the following observations:

1. A large number of pregnant women, infants and children are found to be ingesting well below their needs for energy; some pregnant women are ingesting well below their needs for both energy and protein. For the genetic explanation to account for the observations it would need to be assumed that the genetic and nutritional factors correspond closely with each other and with the corresponding stepwise levels of income. The presumed genetic factors would need to operate differentially, and progressively, in accordance with four different income levels. The mothers would have to (genetically?) limit food intake for themselves and for their child. Correlations among biochemistry, birthweight, and anthropometry would

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all need to accompany both the presumed genetic food causes and the income levels and to progress upwards toward normal in the same stepwise fashion. If genetic factors lower intelligence and that lowers income, there may be a compounding of direct and indirect factors affecting brain development. Food thereby becomes an instrumental factor in the genetic argument.

2. In respect to the possibility that a genetic factor might correlate with race, as has sometimes been proposed, such a factor might be hidden within the survey data but would stand out if the same analyses were carried out separately by race. We therefore examined heights, weights and head circumferences by race and by income.

It is important to begin by recalling that both surveys showed a highly significant excess of small headed children, and that the head circumferences showed gains with increasing family incomes. Within this proviso, how then, do the races, Black, Chicano and White, fare comparatively? The PNS did not have enough Chicanos at any income level to permit their comparison. Blacks and Whites living below poverty had statistically similar populations for height and head circumference, but Blacks were somewhat heavier. There were not enough Blacks at higher income levels in the PNS to make further comparisons. The racial composition of the TSNS did permit making meaningful comparisons among all three races within below poverty and 1-2X poverty groups. For all anthropometric measures, height, weight and head circumference, there were not statistically significant differences between Blacks and Whites except in the below poverty group where Blacks had relatively

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more tall youngsters. Chicanos, relative to the other two races, had more children disadvantaged in all three anthropometric measures, except in the below poverty groups where they were comparable to Whites in height and not dissimilar from Blacks and Whites in weight.

3. Heights of mothers were available for analysis in the PNS. In view of the high heritability of height in healthy, adequately nourished populations, we would expect that if the short stature of PNS children was due mainly to genetic factors then the mothers would be similarly short when compared to growth standards. This was not found to be the case. At every income level the distribution of mothers either met or exceeded height standards.

4. The evidence from Dr. Zee's studies in Memphis seem to us to clinch the matter as far as brain growth and development is concerned. Nutritive supplementation given to an apparently similarly undernourished and stunted population as are manifested in these two surveys but living in Memphis led to a spurt of brain growth among the infants. Increasingly older children in Dr. Zee's population were apparently less responsive to such rehabilitation measures. Infants given nutrition supplementation in Dr. Zee's care departed upwards from their percentile group categories, something they would not normally be expected to do. This is taken to be prima facie evidence that these children were undernourished to the detriment of their brain development. It is also taken to be prime proof that they were previously growing at some rate below their genetic potential. In other words, they needed more food to reach their genetically expected brain growth. Similar

experiences to Dr. Zee's, involving brain growth spurts, even leading to opening of skull sutures, in infants given nutritional supplementation early enough, have been encountered in malnutrition studies abroad. If genetics were used to explain the small head circumferences, we could not expect to encounter brain growth acceleration with any amount of nutritional supplementation. Therefore, to explain the brain growth spurt would require an additional hypothesis, namely, that the children with genetically small head circumference were also sufficiently undernourished to prevent them from living up to their genetic potential. Following nutritional rehabilitation many of Dr. Zee's infants were restored to normal range of head circumferences, thus obliterating any need for the postulated genetic hypothesis.

In conclusion, we have found substantial evidence that more than two million pregnant women, infants, and children under four years of age in the U.S. as of 1970 were undernourished to such a severe degree that the brain development of the unborn and young child was in serious jeopardy. We found evidence that nutritional intake, blood and urinary biochemistry, and anthropometric measures all reveal deficits which tend to be ameliorated as family incomes rise. The presumptive outcome of such chronic, severe undernutrition may be the introduction into the U.S. school systems and ultimately into adult society of between one-third and one-half million youngsters annually (480,000+) who may be lastingly, perhaps permanently, handicapped in relation to functions that depend opon brain structures and organization.

To date there is insufficient information as to the ultimate results of such interference with brain development in terms of

individual achievement and intelligence. Nor is enough known about the possible effects of nutritional intervention in rehabilitating such populations. Note, however, that nutritional rehabilitation, by definition, admits an initial preventable deficient.

Thus far, we have analyzed data relating to the situation as of 1970. It is probable that conditions affecting dietary intakes in the lower socioeconomic populations have not improved in the five intervening years and they they may have worsened because of the rise in cost of living, cost of food, and rate of unemployment.

Finally, we should reconsider the criteria originally selected for predicting jeopardy to brain development. These were deliberately chosen to be conservative criteria. Now using anthropometric data relating to head circumference, we can work backwards independently to venture how many infants and children may have been undernourished to a degree that would induce the observed excess incidence of measurements below standard percentile expectations for head circumference, assuming nutritional factors to be responsible for all of the abnormality. By such a projection, we found that more than two million youngsters may have been severely nutritionally deprived, nearly twice the number predicted on the basis of our nutritional intake criteria. Perhaps a sizable share of this difference is ascribable to the conservatism of our criteria. The range then, of people so affected among pregnant women, infants and children below their fourth birthday, as of 1970, may have been between two and three million, more probably closer to the higher figure. Actual present conditions await an adequate survey and rehabilitation effort where indicated.